

IN THE SPECIFICATION

Please replace the paragraph beginning at 3:9 with the following rewritten paragraph:

Disclosed and claimed herein is a method of stabilizing 17-substituted hydrocortisone compounds, as well as the stabilized 17-substituted hydrocortisone compounds themselves. The method comprises the step of adding a quantity of an omega-6~~3~~ acid to a 17-substituted hydrocortisone composition.

Please replace the paragraph beginning at 3:13 with the following rewritten paragraph:

In a particularly preferred embodiment of the method of the present invention, the omega-6~~3~~ acid comprises linoleic acid. Since linoleic acid is a component of safflower oil, the linoleic acid may be added to the 17-substituted hydrocortisone composition in the form of safflower oil. Safflower oil is, itself, an effective emollient and enhances the skin treatment properties of the stabilized composition. In a particularly preferred embodiment, the safflower oil is added to the hydrocortisone composition in at least equimolar proportion to the hydrocortisone. It has been found that it is highly desirable to add the safflower oil in considerable excess to the proportion of the hydrocortisone, even as much as ten, twenty, thirty or more times as much.

Please replace the paragraph beginning at 4:5 with the following rewritten paragraph:

In addition to the 17-substituted hydrocortisone and omega-6~~3~~ acid, the composition of the present invention may further comprise a number of other compounds typically found in pharmacological hydrocortisone creams and lotions, such as various alcohols, mineral oil, white petroleum, preservative such as BHT, propylparaben and/or butylparaben, citric or other mild acids, sodium citrate, glycerin, fragrances, coloring agents, etc. Generally speaking, the majority of the composition of the present invention will constitute purified water.

Please replace the three paragraphs beginning at 4:13 with the following rewritten paragraphs:

In accord with the present invention, it has been unexpectedly found that the presence of an omega-6~~3~~ acid will inhibit the isomerization of 17-substituted hydrocortisones and other steroid materials. The present invention has particular utility in the stabilization of hydrocortisones having an ester moiety at the 17 position, and is particularly useful in stabilizing HC17-B, and will be described with particular reference to the stabilization of HC17-B.

There are a variety of omega-6~~3~~ acids which function to stabilize the substituted hydrocortisones, and linoleic acid is one particularly preferred acid. Linoleic acid is generally a very safe material, and is readily available. Safflower oil contains large amounts of linoleic acid, and in particular embodiments of the present invention, safflower oil is used as a stabilizing agent for HC17-B and similar materials. Safflower oil is particularly advantageous for use in pharmaceutical compositions, since it is generally nontoxic, and has been approved for both topical and internal formulations. Additionally, safflower oil, as well as other omega-6~~3~~ acid materials, has additional beneficial effects in topical formulations since they can enhance skin penetration and restore lipid content to the skin.

In general, the omega-6~~3~~ acid will be present in an amount which is at least equimolar with the steroid compound which is to be stabilized. In most practical formulations, the omega-6~~3~~ acid is present in a relatively large excess, since it further functions as a skin conditioning agent. For example, it may be present in a weight percentage ten, twenty, thirty or even more times the weight percentage of the steroid compound.

Please replace the two paragraphs beginning at 8:6 with the following rewritten paragraphs:

As can be seen from this data, adding the omega-6~~3~~ acid in the form of the linoleic acid-containing safflower oil considerably increased the

5 stability of the valuable hydrocortisone 17-butyrate compound. In fact, the formulation which did not contain the safflower oil lost approximately 18% of its original HC17-B, whereas the formulation containing the safflower oil lost only approximately 6%. In other words, the improvement in stability was practically threefold. Furthermore, the level of the HC21-B isomer and the other impurities was about 60% less in the formulation containing the safflower oil than in the formulation where the safflower oil was absent.

10 Thus, adding an omega-6~~3~~ acid in the form of the linoleic acid component of safflower oil has been shown to be an effective way of stabilizing 17-substituted hydrocortisone compounds. Of course, while the methods and compositions of the present invention have been described with reference to certain exemplifications and
15 embodiments thereof, the invention is by no means limited to the specifically depicted examples and embodiments. For example, other 17-substituted hydrocortisone compounds could be used with equal efficacy. The omega-6~~3~~ acid could be provided in other forms than as linoleic acid generally, or as safflower oil specifically. It is only
20 necessary that the omega-6~~3~~ acid be provided in a form which is pharmacologically compatible with topical hydrocortisone creams and lotions. Doubtless, one of skill in the art could, after routine experimentation, employ other pharmacologically compatible omega-
25 6~~3~~ components with similar efficacy without departing from the scope of the present invention. It is the claims appended hereto, rather than the exact exemplifications and embodiments, which define the scope of the present invention.